

Cardiac cachexia in cats with congestive heart failure: Prevalence and clinical, laboratory, and survival findings

Sasha L. Santiago | Lisa M. Freeman  | John E. Rush 

Department of Clinical Sciences, Cummings School of Veterinary Medicine, Tufts University, North Grafton, Massachusetts

Correspondence

Lisa M. Freeman, Department of Clinical Sciences, Cummings School of Veterinary Medicine Tufts University 200 Westboro Road North Grafton, MA 01536.
 Email: lisa.freeman@tufts.edu

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Abstract

Background: Cardiac cachexia is common in people and dogs with congestive heart failure (CHF). However, the prevalence and effects of cardiac cachexia in cats are unknown.

Objectives: To determine the prevalence of cachexia and its associations with clinical laboratory and survival data in cats with CHF.

Animals: One hundred twenty-five cats with CHF.

Methods: Medical records of cats evaluated during a 40-month period were retrospectively reviewed to identify cats with cardiac cachexia using 7 different definitions. Clinical, laboratory, and survival data were compared between cats with and without cachexia.

Results: Prevalence of cachexia ranged from 0 to 66.7% for the 7 definitions, with a prevalence of 41.6% using muscle condition score (MCS). Cats with cachexia (determined by MCS) were older ($P < .001$), more likely to have pleural effusion ($P = .003$), had significantly higher blood urea nitrogen ($P < .001$) and neutrophil concentrations ($P = .01$), and significantly lower body condition score ($P < .001$), body weights ($P < .001$), hematocrit ($P = .007$), and hemoglobin concentrations ($P = .009$). Survival time for cats with cachexia (determined by MCS) was significantly shorter than for cats without cachexia ($P = .03$). Cats that were underweight ($P = .002$) and cats with dilated cardiomyopathy (DCM) also had shorter survival times ($P = .04$).

Conclusions and Clinical Importance: The association between cachexia and reduced survival time emphasizes the importance of identifying and addressing this common problem in cats with CHF.

KEYWORDS

cardiology, cardiomyopathy, congestive heart failure, muscle, nutrition

1 | INTRODUCTION

Cardiomyopathies are common in cats, and all can lead to congestive heart failure (CHF). Congestive heart failure not only affects the

Abbreviations: BCS, body condition score; BUN, blood urea nitrogen; CHF, congestive heart failure; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; ISACHC, International Small Animal Cardiac Health Council; MCS, muscle condition score.

cardiovascular system but also has important systemic effects, such as neurohormonal activation, inflammation, and alterations in body composition.¹ Cardiac cachexia is a common systemic effect of CHF and is a complex wasting condition characterized by muscle and weight loss.^{2,3} Cachexia is not specific to CHF and can occur in association with other diseases such as cancer or chronic kidney disease.² Sarcopenia, a related syndrome, is muscle loss associated with aging in the absence of

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disease.^{4,5} In people, the presence of cachexia negatively affects strength, immune function, wound healing, quality of life, and survival.^{6,7}

There is continued debate in the scientific community about the optimal definition for cachexia. Currently, at least 11 definitions of cachexia and 7 definitions of sarcopenia are used in people.^{2,8-19} This discrepancy in definitions affects estimates of the prevalence of cachexia and sarcopenia, with 1 recent systematic review of studies in older people showing that sarcopenia prevalence ranged from 9.9% to 40.4%, depending on which definition was used.¹⁹ In people with heart failure, prevalence rates for cardiac cachexia range from 10.5% to 42%, depending on the definition and the patient population.^{7,20,21} In dogs, the prevalence of cardiac cachexia (based on muscle loss) is 48%-69%.^{22,23} The prevalence of cardiac cachexia in cats with CHF (based on muscle loss) was 48% in one small study.²⁴

Nearly all human definitions of cachexia rely on weight loss as a criterion. This reliance on weight loss for defining cachexia might delay the diagnosis of cachexia since loss of body weight might lag behind loss of muscle and meeting the criterion of weight loss might not occur until late in the underlying disease. One study of people with cancer cachexia, for example, showed that of the patients who did not meet the inclusion criterion of $\geq 5\%$ weight loss over the prior 6 months, 41% had $\geq 5\%$ muscle loss over the same period, suggesting that muscle loss might be a more sensitive measure of cachexia.²⁵ This is particularly true in cardiac cachexia where fluid accumulation can mask weight loss. Another challenge with weight loss as a criterion for the diagnosis of cachexia is that a patient might not have had a body weight measurement in the previous 6-12 months with which to compare to the current body weight. Weight loss might underestimate the prevalence and also might not identify those patients that are most negatively affected by cardiac cachexia. In people with CHF, muscle loss, and not weight loss, is associated with negative effects on strength, function, and quality of life.²⁶

A consistent and sensitive definition could be even more important in veterinary medicine, given the option of euthanasia which can be influenced by factors such as poor appetite, weakness, and quality of life, all common issues in cardiac cachexia. In 1 study of owners of dogs euthanized for CHF, poor quality of life, weight loss, and anorexia were common reasons cited by owners for the euthanasia decision.²⁷ The role of cachexia on the euthanasia decision was not assessed in that study.

The objective of this study was to compare the prevalence of cachexia in cats with CHF using the different definitions available in human and veterinary literature. The hypothesis was that using the definition of cachexia based on muscle loss via muscle condition score (MCS) would identify more cats with cardiac cachexia than other definitions. A secondary objective was to determine clinical and laboratory differences, as well as outcomes, for cats with and without cardiac cachexia.

2 | METHODS

2.1 | Comparison of cachexia definitions

The hospital's electronic medical records system was searched to identify all cats with CHF due to any form of cardiomyopathy evaluated by

the Cardiology Service between June 2015 and September 2018. This starting date was chosen because June 2015 was when the current electronic medical records system was instituted and when MCS began to be collected on all animals during cardiology appointments. An echocardiogram was performed on each cat (GE Vivid 7 Dimension, General Electric Healthcare, Milwaukee, Wisconsin). A board-certified cardiologist or resident under the supervision of a board-certified cardiologist obtained standard right and left parasternal echocardiographic views with standard echocardiographic measurements.²⁸ Cats were determined to have primary myocardial disease (cardiomyopathy) by the attending veterinarian. The diagnosis of CHF was based on the presence of pleural effusion or pulmonary edema confirmed via thoracic radiography or thoracic ultrasound with referable clinical signs, in combination with a diagnosis of cardiomyopathy based on echocardiography. Exclusion factors included cats less than 1 year of age and cats with other major concurrent diseases that could contribute to muscle loss (eg, cancer, preexisting chronic kidney disease), and cats with unregulated hyperthyroidism or systemic hypertension (systolic blood pressure > 180 mm Hg). Cats with CHF due to congenital defects or primary valvular disease, as well as cats with tachyarrhythmia-induced CHF also were excluded.

Medical records were reviewed using a standardized data form to collect the following information from the time of diagnosis of CHF: age, sex, breed, underlying type of myocardial disease, International Small Animal Cardiac Health Council (ISACHC) stage (stage 1 = asymptomatic heart disease, stage 2 = mild CHF, stage 3 = advanced CHF),²⁹ CBC and serum biochemistry results, body weight, body condition score (BCS; on a 9-point scale), and MCS (normal, mild, moderate, or severe muscle loss; Figure 1).³⁰ The BCS and MCS were initially recorded in the medical records by veterinary students but were reviewed and confirmed in all cases by 1 of the cardiologists or cardiology residents. Where available, body weight data from previous visits at our hospital and at primary care veterinarians' hospitals were collected to calculate percent change in weight in the 6 and 12 months before diagnosis and percent change in weight after diagnosis of CHF. The date and cause of death, if not still alive, were also collected. If survival information was not available in the medical record, the primary care veterinarian was contacted or, if any information was still unavailable, the owner was contacted. If the owner could not be contacted, the cat was considered lost to follow-up.

Prevalence of cachexia in cats at the time of diagnosis of CHF was compared using 7 different definitions available in the human and veterinary literature that are applicable to companion animals:

1. Weight loss of at least 5% in the 12 months before diagnosis of CHF (ie, at the time of diagnosis of CHF, cats had already lost at least 5% of their body weight in the previous 12 months) + 3 of the following 5 criteria determined at the time of diagnosis: decreased muscle strength, fatigue, anorexia, low fat-free mass index, or abnormal biochemistry (anemia or low albumin).⁸ Fatigue was defined as lethargy, and decreased muscle strength was defined as weakness noted by the owner.



Muscle Condition Score

Muscle condition score is assessed by visualization and palpation of the spine, scapulae, skull, and wings of the ilia. Muscle loss is typically first noted in the epaxial muscles on each side of the spine; muscle loss at other sites can be more variable. Muscle condition score is graded as normal, mild loss, moderate loss, or severe loss. Note that animals can have significant muscle loss if they are overweight (body condition score > 5). Conversely, animals can have a low body condition score (< 4) but have minimal muscle loss. Therefore, assessing both body condition score and muscle condition score on every animal at every visit is important. Palpation is especially important when muscle loss is mild and in animals that are overweight. An example of each score is shown below.

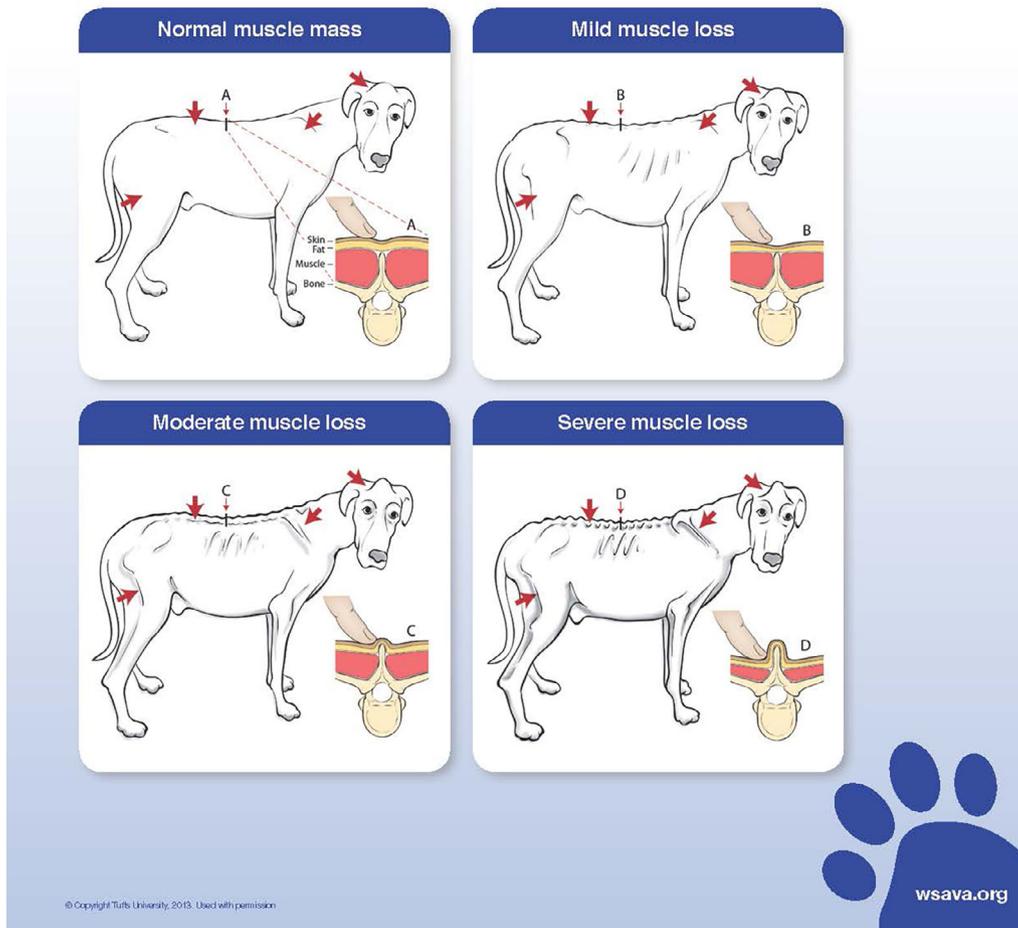


FIGURE 1 Muscle condition scoring system used to evaluate 125 cats with congestive heart failure.³⁰ Provided courtesy of the World Small Animal Veterinary Association (WSAVA). Available at the WSAVA Global Nutrition Committee Nutritional Toolkit website: <https://www.wsava.org/Guidelines/Global-Nutrition-Guidelines>. Accessed November 12, 2019. Copyright Tufts University, 2014

- At least 1 prescription for megestrol acetate, oxandrolone, somatotropin, or dronabinol being taken at the time of diagnosis of CHF or after the diagnosis of CHF.⁹ This definition was modified to include the following veterinary medications: cyproheptadine, mirtazapine, diazepam, or capromorelin (Entyce, Aratana Therapeutics, Leawood, Kansas).
- Greater than or equal to 5% weight loss occurring after the diagnosis of CHF.⁹

4. Weight loss greater than 5% in the 6 months before diagnosis of CHF (ie, at the time of diagnosis of CHF, cats had already lost at least 5% of their body weight in the previous 6 months).¹³
5. Unintended loss of 5% or more of body weight in the 6-12 months before diagnosis of CHF (ie, at the time of diagnosis of CHF, cats had already lost at least 5% of their body weight in the previous 6-12 months).¹⁸
6. Low BCS (<4/9) at the time of diagnosis of CHF.¹⁵
7. Muscle loss based on MCS (ie, mild, moderate, or severe muscle loss) at the time of diagnosis of CHF.^{2,30}

2.2 | Statistical analysis

Data distributions were examined graphically before analysis. Prevalence of cachexia using each of the 7 different definitions was calculated. Chi-square analysis was used to compare categorical variables between cats with and without cachexia. Independent *t* tests (for normally distributed variables) or Mann-Whitney *U* tests (for skewed variables) were used to compare continuous variables between cats with and without cachexia. Survival times were calculated from the time of diagnosis of CHF until the time of death or euthanasia. Cats were right-censored if they were alive at the time of analysis or if they were lost to follow up. Kaplan-Meier curves were constructed, and log-rank analysis was performed to assess the effect of variables on survival. *P* values ≤ 0.05 were considered significant. All statistical tests were carried out using commercial statistical software (Systat, version 13.0, Systat, San Jose, California, and SPSS, version 24, IBM Corp, Armonk, New York).

3 | RESULTS

Between June 2015 and September 2018, 125 cats with CHF met the eligibility criteria. The median age of cats at the time of diagnosis was 10.3 years (range, 1.2-19.6 years), with 89 males (all castrated) and 36 females (35 spayed). The most common breeds included domestic shorthair or longhair ($n = 101$), Maine Coon ($n = 8$), Ragdoll ($n = 3$), Siamese ($n = 3$), Abyssinian ($n = 2$), Sphynx ($n = 2$), and 1 each of Bombay, Burmese, Persian, Scottish Fold, Snowshoe, and Tonkinese. Underlying diseases included hypertrophic cardiomyopathy (HCM; $n = 107$), dilated cardiomyopathy (DCM; $n = 8$), unclassified or restrictive cardiomyopathy (UCM/RCM; $n = 8$), and arrhythmogenic right ventricular cardiomyopathy ($n = 2$). Cats were classified at the time of the original diagnosis of CHF as ISACHC stage 2 ($n = 14$), stage 3a ($n = 32$), or stage 3b ($n = 79$).

At the time of diagnosis, median body weight was 5.0 kg (range, 2.3-10.7 kg) and median BCS was 5 (range, 2-9). Of the 125 cats, 15 (12.0%) were underweight (BCS <4/9), 49 (39.2%) were ideal weight (4-5/9), and 61 (48.8%) were overweight (BCS > 5/9). Fifty-two of the 125 cats (41.6%) had some muscle loss based on the MCS: mild ($n = 31$), moderate ($n = 15$), or severe ($n = 6$). Muscle loss was seen in every BCS category: all 15 underweight cats (100%) had muscle loss, 26 of 49 ideal weight cats (53.1%) had muscle loss, and 11 of 61 overweight cats (18.0%) had muscle loss.

The number of cats with sufficient information on which to determine the prevalence of cachexia based on the different definitions ranged from 18-125 (Table 1). Based on the 7 different definitions, the prevalence of cachexia ranged from 0.0 to 66.7% (Table 1), with

TABLE 1 Prevalence of cachexia in 125 cats with congestive heart failure (CHF) based on 7 different definitions

Definition	Number of cats with information available (%)	Number of available cats meeting definition (%)	Using definition 7 (muscle loss), how many cats were missed
1. Weight loss of at least 5% in the 12 months before diagnosis + 3 of the following 5 criteria at the time of diagnosis: decreased muscle strength, fatigue, anorexia, low fat-free mass index, or abnormal biochemistry (anemia or low albumin) ⁸	18 (14.4)	0 (0.0)	0
2. At least 1 prescription for megestrol acetate, oxandrolone, somatropin, or dronabinol being taken at the time of diagnosis of CHF or after diagnosis. ⁹ This definition was modified to include the following veterinary medications: cyproheptadine, mirtazapine, diazepam, or capromorelin	125 (100)	6 (4.8)	1
3. Greater than or equal to 5% weight loss after diagnosis of CHF ⁹	69 (55.2)	46 (66.7)	28
4. Weight loss greater than 5% in the 6 months before diagnosis of CHF ¹³	28 (22.4)	12 (42.9)	4
5. Unintended loss of 5% or more of body weight in the 6-12 months before diagnosis of CHF ¹⁸	42 (33.6)	19 (45.2)	8
6. Low BCS at the time of diagnosis of CHF (<4/9) ¹⁵	125 (100)	15 (12.0)	0
7. Muscle loss based on MCS at the time of diagnosis of CHF (ie, mild, moderate, or severe muscle loss) ^{2,30}	125 (100)	52 (41.6)	...

TABLE 2 Clinical characteristics and laboratory variables for 125 cats with congestive heart failure at the time of diagnosis

Variable	All cats	Cats with cachexia	Cats without cachexia	P value
n	125	52	73	...
Age (years)	10.3 (1.2-19.6)	12.5 (1.2-18.7)	8.2 (1.2-19.6)	<.001
Sex				.28
Male	89 (89 castrated)	34 (34 castrated)	55 (55 castrated)	
Female	36 (35 spayed)	18 (17 spayed)	18 (18 spayed)	
Disease				.17
HCM	107	42	65	
DCM	8	5	3	
UCM/RCM	8	3	5	
ARVC	2	2	0	
ISACHC classification				.58
2	14	4	10	
3a	32	14	18	
3b	79	34	45	
Body weight (kg)	5.0 (2.3-10.7)	4.4 (2.3-9.2)	5.4 (3.3-10.7)	<.001
Lowest body weight after diagnosis (kg)	4.5 (2.1-10.4)	4.1 (2.1-6.9)	4.9 (2.3-10.4)	.004
Body condition score	5 (2-9)	4 (2-9)	6 (4-9)	<.001
Muscle condition score				<.001
Normal	73	0	73	
Mild	31	31	0	
Moderate	15	15	0	
Severe	6	6	0	
NT-proBNP (pmol/L)	1032 (273 to >1500)	1185 (279 to >1500)	877 (273 to >1500)	.82
Hematocrit (%)	41 (16-63)	39 (16-54)	42 (25-63)	.007
Hemoglobin (g/dL)	13.5 (5.4-21.0)	13.0 (5.4-18.2)	13.7 (8.5-21.0)	.009
WBC (1000/ μ L)	11.7 (4.4-27.4)	14.9 (4.4-27.4)	11.5 (7.8-18.5)	.14
Neutrophils (1000/ μ L)	9.7 (2.1-24.6)	11.5 (2.1-24.6)	9.2 (5.2-14.9)	.01
Lymphocytes (1000/ μ L)	1.1 (.1-5.1)	1.0 (.1-4.4)	1.3 (.1-5.1)	.13
Neutrophils: lymphocytes	8.8 (1.8-96.0)	16.0 (1.8-96.0)	6.6 (1.9-95.0)	.15
Albumin (g/dL)	3.7 (2.6-4.4)	3.7 (2.6-4.1)	3.7 (2.6-4.4)	.96
Globulin (g/dL)	3.5 (2.5-7.9)	3.6 (3.0-7.9)	3.4 (2.5-5.6)	.26
Potassium (mEq/L)	4.2 (2.5-9.0)	4.1 (2.5-9.0)	4.2 (3.0-5.7)	.83
Sodium (mEq/L)	153 (135-161)	152 (135-161)	153 (141-159)	.31
Chloride (mEq/L)	115 (88-134)	115 (88-134)	115 (97-131)	.27
Creatinine (mg/dL)	1.5 (.7-4.6)	1.7 (.7-4.6)	1.4 (.7-2.7)	.31
BUN (mg/dL)	33 (15-112)	36 (17-112)	28 (15-86)	<.001
BUN/creatinine	21 (10-77)	25 (10-77)	19 (10-45)	.007
Glucose (mg/dL)	138 (63-308)	140 (63-277)	138 (69-308)	.19
Cholesterol (mg/dL)	168 (95-348)	168 (95-319)	162 (103-348)	.82

Cachexia was defined as cats with mild, moderate, or severe muscle loss based on the muscle condition score.³⁰ Cats without cachexia had a normal muscle condition score. Data are presented as number of cats or median (range).

Abbreviations: ARVC, arrhythmogenic right ventricular cardiomyopathy; BUN, blood urea nitrogen; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; ISACHC, International Small Animal Cardiac Health Council; NT-proBNP, N-terminal B-type natriuretic peptide; RCM, restrictive cardiomyopathy; UCM, unclassified cardiomyopathy; WBC, white blood cell count.

the lowest prevalence for definition 1 and the highest prevalence for definition 3. Using definition 7 (presence of muscle loss on the MCS), 41.6% of cats had cachexia. Only 42 of 125 cats (33.6%) had body weight recorded in the 6-12 months before diagnosis of CHF (definition 5); for these cats, 19 of 42 (45.2%) had lost $\geq 5\%$ body weight. The median percentage change in body weight in the 6-12 months before diagnosis was -3.3% (range, -22.2% to $+11.6\%$). Sixty-nine of the 125 cats (55.2%) had a body weight recorded after diagnosis of CHF. Using the lowest recorded body weight after diagnosis for these 69 cats, the median percentage change in bodyweight after diagnosis was -11.1% (range, -52.8% to $+15.0\%$). Using muscle loss from the MCS (definition 7), 1 cat identified to have cachexia based on definition 2 would have been missed, 4 using definition 4, 8 using definition 5, and 0 using definition 6 (Table 1). For cats that had body weight information available after diagnosis of CHF, 18 of 26 cats (64.3%) with muscle loss at the time of diagnosis lost at least 5% body weight after diagnosis compared to 28 of 41 cats (68.3%) without muscle loss at the time of diagnosis ($P = .91$).

Since all 125 cats had MCS available and because MCS directly assesses the body compartment most affected by cachexia, all subsequent analyses used definition 7 for categorization of cats with and without cachexia (ie, presence of muscle loss on the MCS). Cats with cachexia were older ($P < .001$), more likely to have pleural effusion ($P = .003$), had significantly higher blood urea nitrogen (BUN; $P < .001$), BUN/creatinine ratio ($P = .007$), and neutrophil concentrations ($P = .01$), and significantly lower BCS ($P < .001$), body weight at the time of diagnosis ($P < .001$), lowest recorded body weight after diagnosis ($P = .004$), hematocrit ($P = .007$), and hemoglobin concentrations ($P = .009$; Table 2).

Thirty-three of the 125 cats were still alive at the time of data analysis, whereas 67 had been euthanized and 17 died; 8 cats were lost to follow-up. Causes of death included worsening CHF ($n = 48$), sudden death ($n = 7$), aortic thromboembolism ($n = 6$), and noncardiac causes ($n = 5$); cause of death could not be determined for 18 cats. Median survival time of cats was 168 days (range, 0-1152 days). For all-cause mortality, cats with cachexia had a significantly shorter survival time (median = 95 days [range, 0-1054 days]) compared to cats without cachexia (median = 281 days [range, 0-1152 days]; $P = .03$; Figure 2). Body condition score also was significantly associated with survival ($P = .02$). Cats that were underweight (BCS $< 4/9$) had significantly shorter survival time (median = 35 days [range, 0-312 days]) compared to cats that were overweight (median = 216 days [range 0-1152 days]; $P = .002$; Figure 3). Survival times were not significantly different between underweight cats and cats with an ideal BCS (median survival = 150 days [range, 0-1127 days]; $P = .07$) or between cats with ideal BCS and overweight cats ($P = .34$). Cats with DCM had a significantly shorter survival time (median = 5 days [range, 0-1152 days]) compared to cats with HCM (median = 168 days [range, 0-1127 days]; $P = .04$). For cardiac mortality, the survival time for cats with cachexia (median = 105 days [range, 0-1054 days]) was not significantly different from that of cats without cachexia (median = 317 days [range, 0-1152 days]; $P = .05$). Underweight BCS ($P = .004$) and DCM ($P = .03$) were significantly associated with shorter survival time. No other variables, including laboratory variables, ISACHC stage, arrhythmia, age,

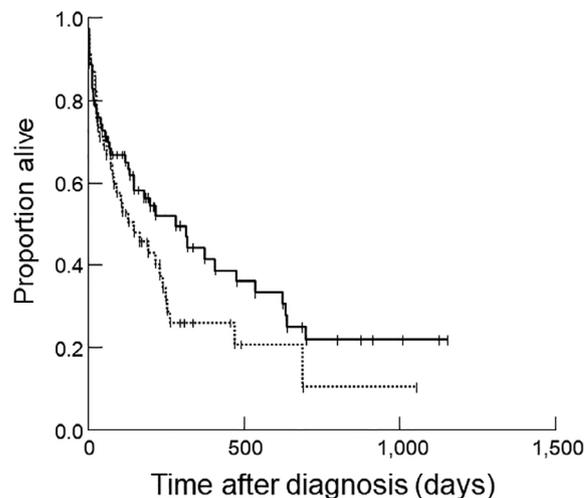


FIGURE 2 Kaplan-Meier survival curve for 125 cats with congestive heart failure stratified by the presence or absence of cachexia, based on having any muscle loss (mild, moderate, or severe) on the muscle condition score. Cats with cachexia (dotted line) had a significantly shorter survival time compared to cats without cachexia (solid line; $P = .03$)

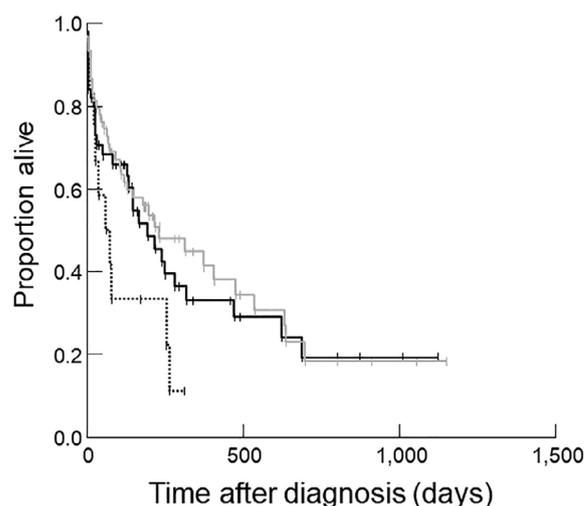


FIGURE 3 Kaplan-Meier survival curve for 125 cats stratified by body condition score (BCS) categories: Underweight cats (BCS $< 4/9$), ideal weight (BCS = 4-5/9), or overweight (BCS $> 5/9$). Cats that were underweight (BCS $< 4/9$; black dotted line) had significantly shorter survival time compared to cats that were overweight (gray solid line; $P = .002$). Survival times were not significantly different between underweight cats and cats with an ideal BCS (black solid line; $P = .07$) or between cats with ideal BCS and overweight cats ($P = .34$)

inappetence, and medications, were significantly associated with all-cause or cardiac mortality.

4 | DISCUSSION

An important challenge in the study of all forms of cachexia is the optimal definition, which has been debated in human medicine for

many years. Although most definitions for cardiac cachexia in human medicine rely on some degree of weight loss, recent research suggests that it is the muscle loss that is more important for the negative effects of cachexia, rather than weight loss alone.^{31,32} In human heart failure patients, those with muscle loss had more functional deficits and reduced quality of life—whether or not they had weight loss—compared to patients with weight loss alone.³¹ Therefore, it is loss of muscle that has the most important clinical implications which supports its role in diagnosis. In addition, results of at least in 1 study of human patients with nonischemic DCM showed muscle loss appeared to occur earlier than weight loss so might be a more sensitive measure of the negative effects of body composition changes in heart failure.³² Therefore, although the optimal definition of cachexia in veterinary and human medicine is not yet known, the current study compared the prevalence of multiple possible options that have been used in the literature in order to begin the conversation on best approaches for identifying cardiac cachexia in cats.

Results of this study showed a wide variation in the prevalence of cachexia in this population of cats with CHF, ranging from 0.0–66.7%, depending on which definition was used. Definition 1 had the lowest prevalence of cachexia and the smallest number of cats with sufficient information available. This is because this definition requires not only weight loss but also 3 of the additional 5 criteria: decreased muscle strength, fatigue, anorexia, low fat-free mass index, or abnormal biochemistry.⁸ Some of these criteria are not routinely assessed in cats (eg, fat-free mass), are difficult to assess (eg, fatigue, muscle strength), or might not have been documented in the medical record (eg, food intake, fatigue), so only 18 cats had sufficient information available and none met all the criteria for this definition. Although the number of cats that could be evaluated using this definition could be improved in future prospective studies by specifically assessing and recording information, it still relies on multiple body weights so likely has limited use in veterinary medicine. Conversely, most cats had information in the medical records to evaluate them for meeting definition 2 (use of appetite stimulants), but only 4.8% of cats met the definition. Therefore, this does not appear to be a good method for identifying cachexia in cats.

The highest prevalence of cachexia was for definition 3 ($\geq 5\%$ weight loss after diagnosis; 66.7%), but this was for weight loss after diagnosis of CHF and used cats' lowest recorded body weights. Therefore, this often measured the loss of body weight long after diagnosis of CHF. The finding that so many cats lost weight after the diagnosis of CHF emphasizes the importance of monitoring body weight, BCS, and MCS throughout the course of disease.

For both definition 4 ($\geq 5\%$ weight loss in the 6 months before diagnosis of CHF) and definition 5 ($\geq 5\%$ weight loss in the 6–12 months before diagnosis of CHF), the prevalence of cachexia was similar (42.9%–45.2%). However, only 22.4%–33.6% of cats had a body weight recorded in the 6–12 months before diagnosis of CHF, so it was impossible to assess most of the cats for weight loss.

In the current study, all 125 cats had BCS (definition 6) and MCS (definition 7) recorded at the time of diagnosis of CHF. Definition 6 (BCS $< 4/9$) yielded a low prevalence of cachexia (12.0%) and did not

appear to be a good approach for identifying cachexia because few cats were actually underweight. In addition, cats in all BCS categories (underweight, ideal, and even overweight) had muscle loss based on MCS. Therefore, waiting until cats become underweight could result in clinically relevant underestimation of muscle loss. Using muscle loss from the MCS (definition 7) at the time of diagnosis of CHF yielded a prevalence of cardiac cachexia of 41.6%. Also, using MCS allows for identification of cachexia at a single point in time (rather than requiring 2 separate body weights) and avoids the requirement for prediagnosis body weight measurements or masking of cachexia by fluid accumulation. The prevalence of 41.6% using MCS from all 125 cats is similar to that reported in 1 smaller study of cats with CHF (48%)²⁴ and in 3 studies of dogs with varying stages of CHF (48%–54%),^{22,23,33} although lower than 1 study which reported a prevalence of 69% in dogs with advanced heart failure due to degenerative mitral valve disease.²³ Prevalence reported in studies of human heart failure ranges from 10.5% to 42% (but is most commonly reported to be approximately 10%).^{7,20,21} In addition, MCS focuses on the body compartment that is most affected by cachexia—muscle—rather than the surrogate of body weight which appears to be less sensitive, might be affected by fluid accumulation, and is less associated in humans with the negative effects on strength, function, and quality of life.²⁶ Therefore, it appears that the MCS is a good clinical method of identifying cachexia in cats.

The only requirement for using MCS to identify cachexia is that clinicians assess MCS at every visit in every cat. This does not obviate the need for also monitoring body weight and BCS at every visit. In the cats for which a follow-up weight was available, 66.7% of cats lost weight after the diagnosis of CHF. The authors find that cats with CHF often need nutritional modification, appetite stimulants, or other nutritional interventions to maintain body weight and muscle as a part of their overall medical care. Results of the current study show that cats can have muscle loss even when they are in ideal body condition or even overweight.

In the current study, cats with cachexia were more likely to have pleural effusion than cats without cachexia. Anecdotally and in 1 study of dogs with DCM and CHF (Freeman LM, Rush JE, unpublished data), dogs with right-sided heart failure are more likely to have cardiac cachexia. One study of human heart failure patients reported an association between elevated right atrial pressure and cachexia³⁴; however, the cause for the association between cachexia and pleural effusion in cats remains to be determined. Cats with cachexia also had a significantly lower hematocrit and hemoglobin concentrations compared to cats without cachexia. This is similar to findings in a small, unpublished study of dogs with cardiac cachexia (Freeman LM, Rush JE. Relationship between cachexia and lymphocyte subpopulations and hematologic parameters in dogs with spontaneously-occurring congestive heart failure. Proceedings of the 3rd Cachexia Conference, Rome, Italy. December, 2005:82). Anemia is 1 of the criteria in the consensus definition of cachexia in humans.⁸ Cats with cachexia were also older and had a significantly higher BUN concentration and BUN/creatinine ratio (but not higher creatinine). Results of a study of clinical and laboratory findings in dogs with cardiac cachexia showed no

significant difference in BUN or creatinine between dogs with and without cardiac cachexia,³³ but that dogs with cachexia had a significantly higher BUN/creatinine ratio (Ineson, Freeman, and Rush, unpublished data). This higher BUN/creatinine ratio could be the result of increased BUN, as can be seen with catabolic states or higher dietary protein intake, or to decreased creatinine concentrations, which can be the result of muscle loss (or a combination of both).³⁵ The higher BUN/creatinine ratio could also be due to early prerenal azotemia (eg, dehydration, diuretic use), or gastrointestinal blood loss, or could be seen in young animals.³⁵ The BUN/creatinine ratio has also been identified in human patients with heart failure and might reflect neurohormonal activation in heart failure.³⁶

Neutrophil concentrations also were significantly higher in cats with cachexia, a finding that was not found in a small, unpublished study of dogs with cachexia (Freeman LM, Rush JE. Relationship between cachexia and lymphocyte subpopulations and hematologic parameters in dogs with spontaneously-occurring congestive heart failure. Proceedings of the 3rd Cachexia Conference, Rome, Italy. December, 2005:82) but was identified in 1 study of dogs with CHF in which cachexia was not reported.³⁷ Laboratory results should be interpreted cautiously, however, because not all cats had laboratory testing the same time in relation to the diagnosis of CHF (eg, measurement before or after initial treatment for CHF). Future prospective studies with a larger population of cats and with standardized laboratory testing would be valuable to further investigate this finding. Cats with cachexia were also older which raises the question of whether some of these cats had sarcopenia instead of or in addition to cachexia. Sarcopenia is loss of muscle associated with aging in the absence of disease.² Since older cats are more likely to have diseases associated with muscle loss (eg, CHF, chronic kidney disease, cancer), there can be concurrent cachexia and sarcopenia.

In the current study of cats, the presence of cardiac cachexia (based on MCS) was significantly associated with a shorter survival time based on all-cause mortality, as has been seen with human^{6,7} and canine studies.³³ However, it is important to note that this study only showed an association between cachexia and shorter survival and did not prove causation. Underweight cats (BCS < 4/9), also had a significantly shorter survival time compared to those that were overweight. This finding requires confirmation since only 15 cats (12.0%) were underweight, but similar findings have been reported in previous studies reporting associations between body weight and survival in cats with CHF and chronic kidney disease,^{38,39} as well as studies on weight loss in dogs with CHF,⁴⁰ and BCS in dogs with chronic kidney disease⁴¹ and cancer.⁴² Although it seems clear that being underweight or losing weight is associated with a shorter survival time, the low prevalence of underweight cats in the current study suggests that clinicians should not wait until cats are underweight to address nutritional status. Evaluating MCS provides a better opportunity to identify cachexia early since 53% of ideal weight and 20% of overweight cats had muscle loss. In addition to associations between BCS and cachexia with survival, cats with DCM had a shorter survival time to those with HCM. Reported survival times for cats with DCM and CHF are very short (median of 11-49 days),^{43,44} whereas reported median survival time for cats with

HCM and CHF ranges from 92 to 564 days.⁴⁵⁻⁴⁷ Other variables might be associated with survival time in cats with CHF, but the small sample size and retrospective nature of the study likely limited the ability to detect other significant associations.

An important limitation of this study was its retrospective nature, so not all of the measurements were available for all the cats and not all were collected at the same time points. This was especially an issue for body weight where in some cases, there were gaps of months to years between recorded body weights. Given that 4 of 7 of the definitions required multiple body weight measurements within a specific time frame, only between 15% and 59% of cats could be included in prevalence calculations using these 4 definitions. Muscle condition score is subjective so, while MCS was assessed only by clinicians on the cardiology service, there could be some interrater variation, as seen in previous studies.^{14,48} Echocardiographic measurements were not analyzed in the current study and would be valuable to include in future, larger studies to determine whether there are any relationships between cachexia, echocardiographic measurements, and outcome. In addition, it is unclear whether all of the weight and muscle loss identified at the time of diagnosis of CHF was due solely to the underlying cardiac disease and not to other diseases or to the muscle loss associated with aging (ie, sarcopenia). Cats with other major concurrent diseases that could contribute to muscle loss, such as cancer, chronic kidney disease, diabetes, or unregulated hyperthyroidism, were excluded from the study, but it is still possible that other undiagnosed disease was present. In addition, since muscle loss (sarcopenia) occurs during aging even in the absence of disease, the weight and muscle loss in these cats at the time of diagnosis could have been related to that, rather than to the underlying cardiac disease. Further research on the time course of weight and muscle loss in cats with cardiomyopathy—both before and after the development of CHF—is warranted. Another limitation is the option for euthanasia in veterinary medicine, which impacts survival time. Finally, the small sample size limited statistical power to detect other differences between cats with and without cachexia and to detect associations between other variables and survival. Nonetheless, results of this study show that measuring muscle loss with the MCS provides the opportunity to detect cardiac cachexia in cats with CHF at a single time point, without having to rely on sequential body weights. Using this simple clinical MCS measurement, 41.6% of cats with CHF met the definition for cardiac cachexia and, more importantly, the presence of cardiac cachexia was associated with a shorter survival time. Further studies on potential methods to prevent and treat cardiac cachexia are warranted, as are methods for promoting the use of MCS as part of the standard physical examination.

CONFLICT OF INTEREST DECLARATION

Within the past 3 years, Dr. Freeman has received research support from Aratana Therapeutics, Nestlé Purina PetCare, and Royal Canin; has consulted with Aratana Therapeutics and Nestlé Purina PetCare; has given sponsored talks for Aratana Therapeutics, Hill's Pet Nutrition, and Nestlé Purina PetCare; and has served on a scientific advisory board for Aratana Therapeutics (all outside the submitted

work). Within the past 3 years, Dr. Rush has received research support from Aratana Therapeutics, Nestlé Purina PetCare, and Royal Canin and has consulted with Aratana Therapeutics and Nestlé Purina PetCare (all outside the published work).

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

ORCID

Lisa M. Freeman  <https://orcid.org/0000-0002-0569-9557>

John E. Rush  <https://orcid.org/0000-0002-8277-8996>

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